Journal of Bacteriology and Parasitology

Kozarov, J Bacteriol Parasitol 2012, 3:3
DOI: 10.4172/2155-9597.1000e103

Editorial Open Access

(Re)Viewing Atherosclerosis as an Infectious Disease - A Key to Personalized Medicine

Emil Kozarov*

Section of Oral and Diagnostic Sciences, Columbia University Medical Center, 630 West 168 Street, P&S Box 20, New York, NY 10032, USA

The availability of open access articles has become a major trend in the biomedical publishing. Nowhere is this approach more important than in the most critical areas of health sciences, the areas where expedited dissemination of knowledge is most crucial, where improved efforts are noticeably rewarded, and where "investment returns" take the form of, among, and in addition to other measures, lifespan extension.

One such critical area is the CardioVascular Disease (CVD). Mortality data show that CVD accounted for 32.8% (811,940) of all 2,471,984 deaths in 2008 in the United States [1]. The commonly accepted risk factors for CVD are hyperlipidemia, hypertension, family history/genetics, smoking, obesity and diabetes. However, infections are not included in this 222-page extensive review on the subject.

Despite meaningful progress in the identification of risk factors and the development of highly effective clinical tools, deaths from CVD continue to increase worldwide. Entirely novel approaches for diagnosis and treatment are needed. Notably, many cardiovascular events have not been explained and many of the individuals with multiple classical risk factors for atherosclerosis have not experienced such event [2]. Myocardial infarction and stroke continue to occur in as many as two thirds of all patients [3].

On the other hand, the literature is replete with examples of epidemiological and seroepidemiological evidence pointing at infections as contributing factor for vasculopathies [4,5]. The notion that the aggregate burden of chronic infections, aggravated by the host immune response plays a major role in atherogenesis led to the recognition of the "pathogen burden" in CVD [1]. However, several large-scale, randomized, controlled clinical trials that were initiated after the cultivation of a bacterial species, *Chlamydophila pneumoniae* from atheromas, did not meet the expectations [6]. Arguably, this cannot dismiss the accumulated epidemiological evidence, or the extensive animal model evidence for infections as a contributing factor in atherogenesis. As an example, the CVD mortality has been found to be related to the number of infections to which a patient has been exposed [7].

There is abundant data demonstrating the existence in the environment of latent, nonreplicating bacteria. The low metabolic activity in this microbial subpopulation, depriving the antibiotics used in the clinical trials from targets, can provide an explanation for the lack of efficiency during the patient treatment. We and others, including a recent paper in this journal have shown the presence of bacterial DNA in atheromatous tissues [8-10]. However, the variety of pathogens whose DNA was identified in the specimens precludes the usefulness of a single drug for bacterial eradication. Most importantly, "DNA does not equal disease". It is easy to identify a bacterial sequence in clinical specimen; it is hard to suggest a clinical relevance. It is only cultivation and identification of live bacterial species from the lesion of disease that fulfills the Koch's postulate and justifies further investigations. We have recently demonstrated the presence of variety of live bacterial pathogens in clinical atherosclerotic specimens, for the first time providing evidence of what might be the most important segment of the human microbiome, the atherosclerosis microbiome [11,12].

The presence of infectious inflammatory agents in such a sensitive location can exacerbate the lesion, provides for a chronicity of the inflammation and may lead to plaque destabilization and rupture, with concomitant life-threatening ischemic events [13].

In the same time, the notion of predictive, preventative, and ultimately personalized medicine is taking hold. Recognizing the infections as a significant contributing factor in atherogenesis and elucidation of the involved specific mechanisms can lead to a relatively inexpensive genomic characterization of the members of the atherosclerotic microbiome. Research in health, communication, and decoding the human genome are … crucial for driving innovation that benefits all of humanity (from the 2012 AAAS Annual Meeting).

Being now able to address CVD as, in a large extent, infectious disease can lead to development of screening devices allowing identification of the underlying infection and determination of the prevalent in the vascular lesion species. Only then an individual treatment regimen with antimicrobials tailored to the specific for the patient organisms can be efficient. The ultimate goal, identification of novel antimicrobial drug candidates for CVD and development of innovative approaches to diagnosis and treatment for atherosclerotic inflammations may then be conceivable, making the most significant step toward personalized medicine. Successfully addressing CVD will undoubtedly alleviate the most complex problem for public health. Of note, biomedical research of atherosclerotic vascular disease as microbial infection is specifically the mission of the Vascular Research Foundation, a first of its kind non-profit organization launched in 2007 "to support medical research reducing the threat of vascular diseases, leading to healthier life" (www.HeartFirst.org).

References

1. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, et al. (2012) Heart disease and stroke statistics- 2012 update: a report from the American Heart Association. Circulation 125: e2-e220.
2. Elkind MS (2010) Infectious burden: a new risk factor and treatment target for atherosclerosis. Infect Disord Drug Targets 10: 84-90.
3. Libby P (2005) The forgotten majority: unfinished business in cardiovascular risk reduction. J Am Coll Cardiol 46: 1225-1228.
4. Epstein SE, Zhu J, Najafi AH, Burnett MS (2009) Insights into the role of infection in atherogenesis and in plaque rupture. Circulation 119: 3133-3141.
5. Frostegård J (2010) Low level natural antibodies against phosphorylcholine: a

***Corresponding author:** Emil Kozarov, Section of Oral and Diagnostic Sciences, Columbia University Medical Center, 630 West 168 Street, P&S Box 20, New York, NY 10032, USA, Vascular Research Foundation, Inc. www.HeartFirst.org, E-mail: EKozarov@gmail.com

Received March 21, 2012; **Accepted** March 22, 2012; **Published** March 28, 2012

Citation: Kozarov E (2012) (Re)Viewing Atherosclerosis as an Infectious Disease - A Key to Personalized Medicine. J Bacteriol Parasitol 3:e103. doi:10.4172/2155-9597.1000e103

novel risk marker and potential mechanism in atherosclerosis and cardiovascular disease. Clin Immunol 134: 47-54.

6. Joensen JB, Juul S, Henneberg E, Thomsen G, Ostergaard L, et al. (2008) Can long-term antibiotic treatment prevent progression of peripheral arterial occlusive disease? A large, randomized, double-blinded, placebo-controlled trial. Atherosclerosis 196: 937-942.
7. Espinola-Klein C, Rupprecht HJ, Blankenberg S, Bickel C, Kopp H, et al. (2002) Impact of infectious burden on extent and long-term prognosis of atherosclerosis. Circulation 105: 15-21.
8. Kozarov E, Sweier D, Shelburne C, Progulske-Fox A, Lopatin D (2006) Detection of bacterial DNA in atheromatous plaques by quantitative PCR. Microbes Infect 8: 687-693.
9. Ott SJ, El Mokhtari NE, Musfeldt M, Hellmig S, Freitag S, et al. (2006) Detection of diverse bacterial signatures in atherosclerotic lesions of patients with coronary heart disease. Circulation 113: 929-937.
10. Wolcott RD, Wolcott JJ, Palacio C, Rodriguez S (2012) A Possible Role of Bacterial Biofilm in the Pathogenesis of Atherosclerosis. J Bacteriol Parasitol 3: 127.
11. Rafferty B, Dolgilevich S, Kalachikov S, Morozova I, Ju J, et al. (2011) Cultivation of *Enterobacter hormaechei* from human atherosclerotic tissue. J Atheroscler Thromb 18: 72-81.
12. Rafferty B, Jönsson D, Kalachikov S, Demmer RT, Nowygrod R, et al. (2011) Impact of monocytic cells on recovery of uncultivable bacteria from atherosclerotic lesions. J Intern Med 270: 273-280.
13. Kozarov E (2012) Bacterial invasion of vascular cell types: vascular infectology and atherogenesis. Future Cardiol 8: 123-138.